REMARKS

Reconsideration is requested.

The specification has been revised in the description of Figure 1 to include a reference to the sequence identifiers of the Sequence Listing, and claim 11 has been revised to include reference to sequence identifiers of the Sequence Listing, in response to the Examiner's comments in §5. on pages 3-4 of the Office Action dated February 16, 2007. The specification is believed to comply with the Sequence Listing rules however the Examiner is requested to contact the undersigned in the event anything further is required in this regard.

The Title has been amended above as suggested by the Examiner. Withdrawal of the objection o the Title is requested.

The Abstract has been amended in response to the Examiner's objection to the Abstract. Withdrawal of the objection to the Abstract is requested.

Claim 18 has been canceled, without prejudice. The objection to claim 18 is moot.

Claims 1-13 and 21-23 are pending. Claims 14-20 have been canceled, without prejudice. Claims 21-23 have been added to define further patentable aspects of the disclosure. No new matter has been added.

The Section 112, second paragraph, rejection of claims 1-13 is traversed. The Section 112, second paragraph, rejection of claim 18 is moot in view of the above. Reconsideration and withdrawal of the rejection of claims 1-13 are requested in view of the following comments.

The Examiner is understood to believe that the phrases "high salt lysate" and "high-salt-detergent", in the claims render same indefinite as the Examiner is understood to believe these phrases are relative terms. The applicants believe that while it may be the case that in isolation the terms are relative, the applicants believe that in the context of claim 1 the terms are labels or placeholders presented to define the compositions obtained at the end of steps (c) and (d) respectively. In other words, the applicants believe that the term "high-salt" buffer is the buffer comprising the salt-buffer as defined in step (b) of claim 1 following the lysis of the cells which are suspended in the buffer defined in step (b). Likewise, the applicants believe that the term "high-salt-detergent" would be understood by one of ordinary skill in the art as "high-salt-detergent lysate", i.e. the lysate of step (c) to which a detergent has been added.

The applicants believe that the use of the two terms will be understood by one of ordinary skill in the art to provide clarity to the recited steps of claim 1, which is defined in structural terms by reference to the salt buffer having a specified concentration. The claims are believed to be definite in this regard.

The Examiner is understood to believe that the recitations of "high-salt detergent" and "high-salt-detergent buffer" are indefinite. Claim 4 has been amended in a manner similar to claim 1, without prejudice, making moot the rejection.

The Examiner is further understood to believe that the phrase "rapidly desalting" of claim 4 is unclear without a point of reference. The applicants submit that claim language, including terms of degree, which may not be precise, is not automatically indefinite in the context of Section 112, second paragraph. See Seattle Box Co., v.

Industrial Crating & Packing, Inc., 221 USPQ 568 (Fed. Cir. 1984). Acceptability of the claim language depends on whether one of ordinary skill in the art would understand what is claimed, in light of the specification. The applicants believe that the specification teaches that rapid desalting is a process which is generally something that takes place on a column with a relatively high flow rate such that the desalting occurs in less than about 30, e.g. less that about 10, minutes. The specification contrasts this with a process such as dialysis, which is usually practiced in the art over a period of many hours or days. The specification further notes that a prolonged desalting process is believed to lead to aggregation and denaturation of P450, which is avoided by the use of a rapid, column based process.

One of ordinary skill in the art will appreciate the metes and bounds of the claimed invention, in view of the specification and generally advanced level of skill in the art. The precise flow-rate of a column may depend upon several factors, including the size of the column and amount of protein loaded. However, such factors can be determined routinely without undue burden by those of ordinary skill in the art.

As noted in the MPEP, Section 2173.05(b), when relative terms are used in claims wherein the improvement over the prior art rests entirely upon size or weight of an element in a combination of elements, the adequacy of the disclosure of a standard is of greater criticality. In the present invention, the term "rapidly desalting" is used in a dependent claim which is dependent on a claim believed to be clearly distinguished over the art for the reasons set out herein.

The term is believed to be consistent with the general level of skill in the art, and does not present the ordinarily skilled person with any difficulty.

The Examiner is understood to have requested clarification of the term "N-terminal membrane inserting element" in claim 10. The pending claims are believed to be definite in this regard.

Withdrawal of the Section 112, second paragraph, rejections is requested.

The Section 112, first paragraph "written description" and "enablement", rejections of claims 10-11 are traversed. Reconsideration and withdrawal of the rejections are requested in view of the following comments.

The applicants submit, with due respect, that the Examiner's basis for the rejections fail to properly characterize the state of the art and knowledge of the biology of P450s. Page 278 of Kempf (Arch. Biochem. Biophys., 1995, 321, 277-288), for example, provides an overview in the following terms:

> According to the currently accepted model for the topology of P450s inserted into the membranes of the endoplasmatic reticulum, a short, highly hydrophobic N-terminal segment acts as a noncleavable signal sequence for the signal recognition particle (9). It is generally believed that the remainder of the P450 protein, including the C-terminal heme-binding domain, assumes a globular structure which protrudes into the cytoplasmic space (10-12). This model suggests that the globular domain of microsomal P450s may be less hydrophobic and more soluble. Deletion of the N-terminal segment in conjunction with high-level heterologous expression could thus provide the means to obtain preparative amounts of soluble mammalian P450 forms which may be easier to study and could probably even be crystallized.

This overall gross structure of P450s is also reflected by the teaching of Szklarz et al (J. Computer-Aided Mol. Des., 11, 265-272 (1997), of record) which on page 266

shows an alignment of the human 3A4 P450 protein with four bacterial P450s. The Examiner will note that although the primary sequence of 3A4 is very different from that of the bacterial enzymes, the authors have presented an alignment based on structurally conserved helical domains (A-L) and regions of beta sheets. These domains start following the N-terminal region of the proteins. It can clearly be seen that the 3A4 protein contains an extended N-terminal region rich in hydrophobic amino acids, in accordance with the teaching of Kempf et al.

In addition to the state of knowledge in the art at the time of the instant application, the present specification teaches numerous examples of deletions of the N-terminal region of P450s by others. Thus at pages 5-6 of the instant specification it is stated:

> Several attempts to produce soluble mammalian cytochrome P450s by removing the N-terminus have been reported in the literature by different groups. Similar N-terminal deletions of cytochrome P450s have been used in each case...

Page 6, second paragraph, of the specification further provides the following:

> This group (Wachenfelt et al., 1997, Arch. Biochem. Biophys. 339, 107-114; Cosme et al., 2000, J. Biol. Chem. 275, 2545-2553) have expressed the rabbit 2C3 and 2C5 isoforms in E. coli with residues 3-21 at the N-terminus deleted.

Following a summary of the teaching of Kempf et al on page 6, the specification at page 7 teaches:

> Gillam et al, (Gillam et al., 1995, Arch. Biochem. Biophys. 319, 540-550), have examined a series of N-terminal

> modified constructs of human cytochrome P450 2D6 for expression in E. coli. Although several of these produced some cytochrome P450 2D6, there was considerable variation in the expression rate. The best construct involved the removal of the N-terminal hydrophobic region. ...
>
> Pernecky et al. (Pernecky et al. Proc. Natl. Acad. Sci. USA, 1993, 90, 2651-2655) have expressed the rabbit N-truncated forms of cytochrome P450 2B4 and 2E1 and several chimeras in E. coli.

Page 8 of the specification teaches the following:

> Larson et al. (Larson et al., 1991, J. Biol. Chem, 266, 7321-7324) found that rabbit cytochrome P450 2E1 expressed in E. coli without amino acids 3-29, like the full-length cytochrome P450, was predominantly in the membrane fraction.
>
> Saraga et al. (Saraga et al., 1993, Arch. Biochem. Biophys. 304, 272-278) have expressed a truncated form of the bovine microsomal 17β-hydroxylase cytochrome P450 (P450c17) lacking its N-terminal hydrophobic signal anchor sequence (residues 2-17).

The applicants submit that the general level of skill in the art is advanced and that one of ordinary skill in the art will appreciate from the present specification and the advanced level of skill in the art that the applicants were in possession of the claimed invention at the time the application was filed. The ordinarily skilled artisan will also be able to practice the claimed invention, without undue experimentation, given the teachings of the present specificaiton as well as the generally advanced level of skill in the art.

The applicants urge the Examiner to appreciate the findings of the Federal Circuit in Capon v. Eshhar, 76 USPQ2d at 1084, that the description of a specification needed

to satisfy the written description requirement

> varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence.

The applicants believe that in the case of inventions relating to the use of known genetic sequences, Section 112, first paragraph, does not require that the structure of formula of such sequences are set out in the specification. The Examiner will appreciate that that which is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. The teaching of the art summarized above shows that, for example, the art recognized that an N-terminal region of P450s could be recognized in a location N-terminal to the start of recognized folded domains of this class of proteins, and that truncation of proteins at this region was commonly practiced.

Claims 10 and 11, are submitted to be supported by an enabling disclosure which also demonstrates that the applicants were in possession of the claimed invention at the time the application was filed.

Withdrawal of the Section 112, first paragraph, rejections of claims 10 and 11, are requested.

The Section 112, first paragraph "written description" and "enablement", rejections of claim 13 is traversed. The Section 112, first paragraph "written description" and "enablement", rejections of claim 18 is moot in view of the above. Reconsideration and withdrawal of the rejections of claim 13 are requested in view of the following comments.

Claim 13 as amended relates to the crystallization of a P450 selected from the group consisting of P450 2C9, P450 2C19, P450 2C19-1B, P450 2D6 and P450 3A4. It

is understood the Examiner's objection does not extend to these species and thus the rejection is traversed by the amendment to claim 13, without prejudice.

The Examiner's indication that the specification is enabling for a method of crystallizing cytochrome P450 2C19 wild type (SEQ ID NO: 2) having space group of P321, cell dimensions of a=158 Å, b=158 Å, c=212 Å and α=90°, β=90°, γ=120°, and P450 3A4 (SEQ ID NO: 8) having the space group C2 and the unit cell dimensions a=l52 Å, b=101 Å, c=78 Å and α=90°, β=120°, γ=90°, is acknowledged with appreciation.

The applicants believe that the present specification provides extensive teachings of a range of crystallization conditions suitable for the crystallization of different P450 proteins. Pages 25-27 of the present specification, for example, provide detailed teaching of buffer conditions and crystallization methods useful for the preparation of crystals of cytochrome P450 molecules. The protein 2C19 was crystallized against a range of 75 sets conditions, recited on pages 37-39. All such conditions produced crystals of the protein.

Page 40 of the present specificaiton provides one set of conditions for crystallization of 2C9, and also described on this page through page 44 is a method for the crystallization of P450 2C19-1B, under 14 sets of different conditions. 2D6 was also crystallized under a range of 20 sets of different conditions (pages 54-55) and crystals were formed. Finally, on pages 61-62 crystals of 3A4 were produced under 30 sets of crystallization conditions. Thus in all, about 140 specific different crystallization conditions are illustrated in the specification, in addition to the extensive generic teaching of on pages 25-27.

The applicants submit, with regard to claim 13 for example, there is no requirement that the crystal has any specific diffraction quality is recited. As noted above, the present specification teaches a wide variety of different conditions for the purification and crystallization of cytochrome P450 proteins, including but not limited to the species recited in instant claim 13. In the light of such teaching, it is submitted that those of ordinary skill in the art would be able to perform the crystallization of a P450 selected from the group of P450 2C9, P450 2C19, P450 2C19-1B, P450 2D6 and P450 3A4 based on the teaching pages 25-27 and numerous specific examples referred to above.

Claim 13 is submitted to be supported by an enabling disclosure which also demonstrates that the applicants were in possession of the claimed invention at the time the application was filed.

Withdrawal of the Section 112, first paragraph, rejections of claim 13 is requested.

The Section 102 rejection of claims 1-4, 6-8 and 10 over Kempf (1995, Archives of Biochemistry and Biophysics, vol. 321, p 277-288, as cited in the IDS) as evidenced by Sigma catalog (H7637 HEPES hemisodium salt) and Calibiochem catalog (Calbiochem 205534) is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

Claim 1 recites that the in step (b) that the cells are recovered from culture and suspended in a salt buffer having a salt concentration of from 200 to 1000 mM and a conductivity of from 12 to 110 mS/cm.

Kempf et al refers to a process for recovery of a P450 2D6 protein in which cells

are suspended in a buffer comprising 150 mM NaCl and 50 mM Hepes. The Examiner has characterized the latter as "NaHepes", as based on the citation of the Sigma catalogue. The Examiner's attention is drawn to the footnote on page 278 of Kempf, in which the abbreviations of the disclosure are set out. "Hepes" is defined as "N-[2-hydroxyethyl]-N'-[2ethanesulfonic acid]". It is the acid form of Hepes therefore which is used in the cited art.

Attached herewith is page 897 of the 1999-2000 Aldrich catalogue which shows that both the acid and sodium salt form of Hepes are known in the art. Kempf et al used the acid form. Hepes is used as a buffering agent. As noted in the Aldrich catalogue, Hepes is a "Buffer used in the physiological pH range".

Accordingly, the salt concentration in Kempf in the resuspension and lysis step is 150 mM NaCl. Claim 1 requires a salt concentration of from 200 mM to 1000 mM and a conductivity of from 12 to 110 mS/cm. Accordingly, the claims are not anticipated by Kempf and withdrawal of the Section 102 rejection is requested.

The Section 103 rejection of claim 5 over Kempf (1995, Archives of Biochemistry and Biophysics, vol. 321, p. 277-288) in view of Anderson (1968, Journal of Bacteriology, vol. 96, p 93-97) is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

Kempf et al is understood to be directed to methods of purifying P450 proteins following recombinant expression. As noted above, Kempf et al does not anticipate the presently claimed invention. Nor is the presently claimed invention rendered obvious by Kempf et al. alone or in combination with Anderson

In particular, as can be seen from Table 1(B) on page 282 of Kempf et al, the recovery of P450 2D6 in the presence of detergent was 21%. Tables 1 and 2 of page 28 of the present specification describe that the recovery of P450 by the procedure of the present invention was about 4-fold higher. Further, the protein recovered by the presently claimed invention was in a form suitable for crystallization.

Though Kempf et al may seek to provide proteins for crystallization, the reference is understood to teach that proteins purified by omission of a detergent are aggregated and thus unsuitable for crystallization whereas the ability of the detergent-purified form is not reported.

It is further noted that the detergent-based purification method of Kempf results in the co-elution of a 30kDa protein (page 279 column 2) which required two further column purification steps (DEAE-Sephacel and HA columns) to remove.

The present applicants were able to obtain purified P450 protein for crystallization without the need to undertake these additional steps.

A further distinction between Kempf et al and the present invention is in the purification of P450 from a cell culture in a high salt buffer having a salt concentration of from 200 mM to 1000 mM and a conductivity of from 12 to 110 mS/cm. As explained in the present specification at page 9, the present applicants believe that there was a perceived need in the art to resuspend host cells expressing P450s in a buffer with low ionic strength prior to lysis. This belief is consistent with the teaching of, *inter alia*, Kempf et al, which uses only 150 mM NaCl.

In addition, as taught by Kempf et al, because of the lower ionic strength buffer, the P450 protein had to be recovered from a membrane fraction. Thus at page 279

column 2, Kempf et al teach that after lysis in the 150mM NaCl buffer the resulting supernatant (minus cell debris) was centrifuged at 142,000*g* for 1 hour and the pellet (designated the membrane fraction) was resuspended in 500 mM NaCl, and then recentrifuged at 142,000*g* for a further hour.

The present applicants have discovered that by increasing the ionic strength of the salt buffer in which the cells are lysed recovery is improved. As noted in the present specification at page 9, it was perceived necessary in the art to resuspend host cells expressing P450s in a buffer with low ionic strength prior to lysis. The present applicants have discovered that by using a higher ionic strength buffer at the time of lysis, the yield of protein in a non-aggregated state is increased.

The applicants urge the Examiner to note that on page 279, first column, of Kempf et al the citation teaches the purification of a 2D6 protein in the absence of a detergent. Cells were lysed in a low-salt buffer, containing 5 mM $MgCl_2$, 50 mM NaCl and 50 mM potassium phosphate buffer. Only after the homogenate had been centrifuged at 142,000*g* for 1 hour was a high salt buffer (500 mM NaCl) used to resuspend the membrane fraction. Following purification of the P450, it was found that most of the protein was in an aggregated state - see Abstract, Results on page 283 and Discussion. This aggregated form was unsuitable for crystallization - see Discussion, final paragraph. To address this problem, Kempf et al is understood to have proposed a purification process in which detergent was added after the membrane fraction was resuspended in a 500 mM salt buffer. However, Kempf et al still used a buffer with only 150 mM NaCl in which to lyse the cells. Only after lysis and centrifugation to recover a membrane fraction was a high salt buffer used.

In the present invention, the inventors have discovered that by using a buffer with a high ionic strength in the initial cell lysis step it was possible to recover P450 without the need to recover a separate membrane fraction. This eliminates a step of the recovery process and, as noted above, increases the overall yield of the protein. The recovered protein is suitable for the production of crystals. Though at least one of the aims of Kempf et al was to provide proteins in a form for crystallization (see Introduction, last sentence and final paragraph of discussion), there is no indication that the protein recovered by the Kempf procedure was, or could be, crystallized.

There is no teaching in Kempf et al to use a high ionic strength buffer during the cell lysis step. Kempf et al do use a high ionic strength buffer during later stages of the recovery process, but explicitly do not use the buffer during the initial step.

Moreover, with respect to presently pending claim 4, the applicants urge the Examiner to note that the high-ionic strength fraction of Kempf et al is applied to an affinity support column which is rinsed and then used to elute protein with a wash and elution buffer based on buffer AD, which is understood to be defined as comprising, unless otherwise specified, 150 mM NaCl and 50 mM Hepes.

In contrast, claim 4 of the present application involves the use of high-salt buffers having a salt concentration of from 200 mM to 1000 mM and a conductivity of from 12 to 110 mS/cm for the rinsing and elution steps, followed by rapid desalting. As noted above, Kempf et al report the co-elution of a 30 kDa protein from their procedure. In contrast, the procedure of the invention provided sufficiently pure, monodisperse P450 to allow for crystallization.

The cited Anderson reference fails to cure these deficiencies of Kempf.

Withdrawal of the Section 103 rejection is requested.

The Examiner is requested to hold the provisional obviousness-type double patenting rejection of claims 1-12 over claims 1-12 of copending application Serial No. 10/221,036 in abeyance until such time as allowable subject matter is identified.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned in the event anything further is required.

Respectfully submitted,

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ABSTRACT

The invention provides a method for the purification of cytochrome P450 molecules, particularly human P450 molecules including 2C9, 2C19 and 2D6, the method comprising expressing in a host cell culture a cytochrome P450 molecule; recovering said cells from said culture and suspending said cells in a high salt buffer; lysing said cells and removing cell debris to provide a high-salt lysate; adding to said lysate a detergent to provide a high-salt-detergent lysate; and recovering said P450 from said lysate. The method provides yields of P450 proteins suitable for crystallization.

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ABOUT THE COVER

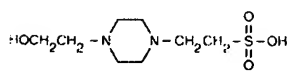
The Apostle Paul (oil on canvas 51¾ x 41⅝in.) was painted by Rembrandt van Rijn (1606-1669) about 1657. Paul seems to have fascinated Rembrandt throughout his career; the artist represented him as early as 1627 in a painting of *Saint Paul in Prison*, and as late as 1661, when he painted himself as Saint Paul.

Probably executed with at least some participation by an assistant, this painting is a superb example of Rembrandt's later style. In his earlier works, details were carefully delineated, subjects normally shown in an identifiable environment, and the apparent source of light specifically located. In *The Apostle Paul*, there is no sense of a particular setting, details are minimized, and the light on Paul's face, hands, and on the folio before him does not come from a readily identifiable source. Aside from the chair and the desk, only the quill, the book, and the sword behind the desk are recognizable. Here Rembrandt does not use light and shade primarily to define form but to express moods and spiritual meaning. As the art historian Wilhelm von Bode said early in this century, Rembrandt's later works rendered "souls rather than...existences."

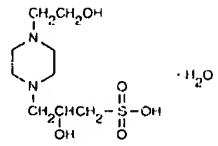
This painting is in the Widener Collection at the National Gallery of Art in Washington, D.C.

If you would like a reproduction of this painting, we will be happy to send you a full-color print (11 x 14in.) for £3.20 (to cover postage and handling). Please request Z25,188-7 and specify *The Apostle Paul* from the cover of the 1999-2000 Aldrich Catalogue. You can also contact us for a list of paintings that have appeared in Aldrich publications and are available as full-color prints.

			£
21,966-5	★	**Heneicosanoic acid,** 99% [*2363-71-5*] $CH_3(CH_2)_{19}CO_2H$ FW 326.57 mp 74-75° ..... *Beil.* 2(1),179 *FT-NMR* 1(1),758B *FT-IR* 1(1),486B *SI* 75.C,8 *Safety* 2,1813C *R&S* 1(1),537B	250mg 1g	33.50 93.00
24,923-8		***cis*-9-Heneicosene,** 97% [*39836-21-0*] $CH_3(CH_2)_{10}CH{=}CH(CH_2)_7CH_3$ FW 294.57 .... n^{20}_D 1.4500 Fp 144°F(62°C) *FT-NMR* 1(1),28C *FT-IR* 1(1),21A *SI* 3,E.3 *Safety* 2,1814A *R&S* 1(1),21G	1g 5g	29.20 108.30
16,371-6	★	**HEPES,** 99% [*7365-45-9*] [4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid]. FW 238.31 mp 234°(dec.) *Merck Index* 12,4687 *FT-IR* 1(1),893B *SI* 165.D.4 *R&S* 1(1),1061K *RTECS#* TL6809000 Buffer useful in the physiological pH range. *J. Org. Chem.* **1993,** *58,* 2663. *Am. J. Physiol.* **1993,** *264,* C27. *Aldrichimica Acta* **1983,** *16,* 35. p K_a = 7.35 ± 0.10 at 20°C	10g 25g 100g	6.10 12.20 34.70
23,388-9	★	**HEPES, sodium salt,** 99% [*75277-39-3*] [4-(2-hydroxyethyl)-1-piperazineethane-sulfonic acid, sodium salt] FW 260.29 *FT-IR* 1(1),893C *SI* 165.A,5 *Safety* 2,1815D *R&S* 1(1),1061L *HYGROSCOPIC*	10g 25g 100g	8.30 13.50 35.60
44,249-6	★	**HEPPSO** [*68399-78-0*] [3-hydroxy-4-(2-hydroxyethyl)-1-piperazinepropane-.....sulfonic acid monohydrate] FW 286.35 mp >158-160°(dec.) *Beil.* 23(5),2,389	25g 100g	23.40 75.30
25,731-1	★	**1,1,1,2,2,3,3-Heptachloropropane,** 99% [*594-89-8*] $C_2Cl_5CHCl_2$ FW 285.21 ..... mp 29-30° bp 165-166°/90mm Fp none *Beil.* 1,108 *FT-NMR* 1(1),131B *FT-IR* 1(1),91A *SI* 10.C,10 *Safety* 2,1816C *R&S* 1(1),91E R: 36/37/38 S: 26-37/39	25g 100g	26.70 67.50
		Heptacosafluorotributylamine, see 28,094-1, Perfluorotributylamine page 1331		
28,606-0	★	**Heptacosane,** 99% [*593-49-7*] $CH_3(CH_2)_{25}CH_3$ FW 380.75 mp 59-61° bp 270°/15mm *Beil.* 1,176 *SI* 1.B,6 *R&S* 1(1),7A	5mg 25mg	13.70 39.70
34,018-9	★	**Heptacosanoic acid,** 98% [*7138-40-1*] $CH_3(CH_2)_{25}CO_2H$ FW 410.73 mp 88-89° ..... *Beil.* 2(3),1094 *SI* 75,D,9 *R&S* 1(1),537G	100mg 250mg	19.60 42.10
47,767-2	NEW	**1,3,5,7,9,11,14-Heptacyclohexyltricyclo[7.3.3.1^{5,11}]heptasiloxane-3,7,14-triol,** ..... 97% [*47904-22-3*] FW 973.70 mp 109° *MOISTURE-SENSITIVE*	1g	43.20
47,765-6	NEW	**1,3,5,7,9,11,13-Heptacyclopentyl-15-[2-(diphenylphosphino)ethyl]penta-..... cyclo[9.5.1.1^{3,9}.1^{5,15}.1^{7,13}]octasiloxane** (diphenylphosphinoethyl-POSS) FW 1,113.82 mp 260-268° *MOISTURE-SENSITIVE* Use governed by U.S. Patents 5 484 647 and 5 412 053 and other pending patents	1g 5g	38.40 168.00
47,760-5	NEW	**1,3,5,7,9,11,13-Heptacyclopentyl-15-glycidylpentacyclo[9.5.1.1^{3,9}.1^{5,15}.1^{7,13}]-..... octasiloxane,** 95% (glycidyl-POSS) FW 957.65 mp >350° *MOISTURE-SENSITIVE* Use governed by U.S. Patents 5 484 647 and 5 412 053 and other pending patents	1g 5g	33.60 152.00
47,762-1	NEW	**3,5,7,9,11,13,15-Heptacyclopentylpentacyclo[9.5.1.1^{3,9}.1^{5,15}.1^{7,13}]octasiloxane-1-butyronitrile,** 98% (3-cyanopropyl-POSS) FW 968.67 mp 300°(dec.) *MOISTURE-SENSITIVE* R: 20/21/22 S: 36 Use governed by U.S. Patents 5 484 647 and 5 412 053 and other pending patents	1g 5g	33.60 152.00



16,371-6



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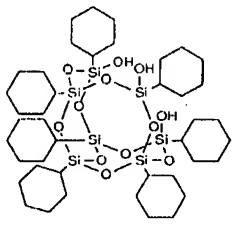
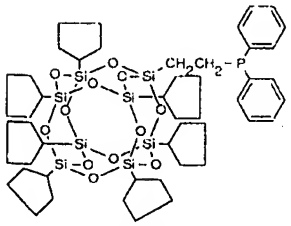
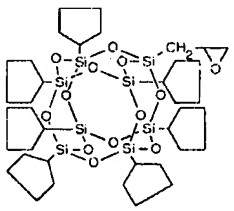


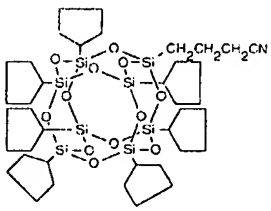
47,767-2



47,765-6



47,760-5



47,762-1